Here we describe a 6-year observation of the disease. More than 3 years of remission may be observed. Moreover, although PRCA relapsed in October 1993, without any manifestations of CLL, it was again successfully treated by the six CVP courses. The patient has since then been in remission for over 1 year.

The remission of this PRCA was consequently judged to depend on cytotoxic chemotherapy. Similarly, some authors reported that CLL with PRCA treated successfully by chemotherapy may relapse without additional maintenance therapies, and long-term chemotherapy may be necessary [2,3]. We believe that any cases of PRCA for which cytotoxic chemotherapy is used will require a careful long-term follow-up.

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References

1. Krantz S, Dessypris EN: Pure red cell aplasia. In Golde DW, Takaku F (eds): "Hematopoietic Stem Cells." New York: Marcel Dekker, 1985, p 229.
2. Chikkappa G, Pasquale D, Phillips PG, Mangan KF, Tsan M-F: Cyclospolin-A for the treatment of pure red cell aplasia in a patient with chronic lymphocytic leukemia. Am J Hematol 26:179, 1987.
3. Hocking W, Champlin R, Mitsuyasu R: Transient response of pure red-cell aplasia to anti-thymocyte globulin in a patient with T-cell chronic lymphocytic leukemia. Am J Hematol 24:285, 1987.
4. Hara T, Mizuno Y, Nagata M, Okabe Y, Taniguchi S, Harada M, Niho Y, Oshimi K, Ohga S, Yoshikai Y, Nomoto K, Yumura K, Kawa-Ha K, Ueda K: Human γβ T-cell receptor-positive cell-mediated inhibition of erythropoiesis in vitro in a patient with type 1 autoimmune polyglandular syndrome and pure red blood cell aplasia. Blood 75:941, 1990.
5. Maung Z-T, Norden J, Middleton PG, Jack FR, Chandler JE: Pure red cell aplasia; further evidence of T cell clonal disorder. Br J Haematol 87:189, 1994.

Acute Megakaryo-Monocytic Leukemia With Acute Myelofibrosis

To the Editor: Myelofibrosis (MF) is thought to be a secondary reaction to hematological malignancy [1,2]. In this report, we report on a case of AMF in which there were no morphologically abnormal blasts but many abnormal cells expressing megakaryocytic and monocytic markers.

A 60-year-old male was admitted on September 21, 1994 because of fever and pancytopenia. He was well until June 1995, when fever recurred. He was admitted to a local hospital where thrombocytopenia was pointed out. He was referred to our hospital. Physical examination showed petechiae in the extremities. Hematological examination showed pancytopenia (WBC 1,200/μl, Hb 10.3 g/dl, PLT 2.0×10^4/μl), and there were neither myeloblasts nor leukemic cells in peripheral blood. In a surface-marker examination of peripheral blood, there were many CD41a-positive cells in nonlymphoid cells (Table I). A bone-marrow biopsy specimen showed severe myelofibrosis with a small hypercellular area containing granulocyte-series hyperplasia. Prednisolone was not effective. In October, dark-green nevoid eruptions appeared in the face and trunk. Biopsy specimens of these regions showed invasion of lysozyme-positive blasts. In November, nonbacterial arthritis of the bilateral hip joints appeared, and their synovia contained many CD11b-positive cells that were also esterase-positive. Low-dose Ara-C (LDAC) therapy and BHAC-DMP therapy were not effective. Chemotherapy of dexamethasone (10 mg/day) and Ara-C (30 mg/day) was started on February 21, 1996. After 6 days of this therapy, all eruptions had disappeared. Dexamethasone and Ara-C were decreased to levels at which the leukocyte count in peripheral blood was stable, and Ara-C was exchanged for cytarabine ocfosfate. He was then discharged.

Many cases of AMF are accompanied by acute megakaryocytic leukemia, of which blasts are characterized by platelet peroxidase, immunohistochemical stains, and monoclonal antibodies against platelet antigens, although it has been reported that flow-cytometric CD41a expression is sometimes false-positive [3]. Inappropriate growth-factor release from megakaryocytes was recognized as a mediator of fibrogenesis [4]. PDGF and TGF-β are especially important cytokines [5].

In this case, bone-marrow biopsy showed severe MF. Myeloid mature cells in the patient's peripheral blood abnormally expressed CD41a. In the biopsy specimen of skin eruption and synovia, there were many dysplastic mononuclear cells which had monocytic characters. These invasions were suggestive of acute leukemia. In examination of surface markers of peripheral leukocytes, there were morphologically normal cells which simultaneously expressed two or three markers of megakaryocytic, myelocytic, and monocytic markers. Platelets did not adhere to these cells in immunohistochemical stains of CD41a. They were thought to be abnormal cells. These cells, which showed mixed or biphenotypic differentiation, were thought to induce MF with some cytokines. Therefore, this case may be important regarding considerations of megakaryo-monocytic differentiation and MF pathogenesis due to megakaryo-monocytic abnormalities.

On the other hand, AMF has very poor prognosis. In this case, the combination LDAC and dexamethasone therapy was effective, although LDAC or prednisolone alone was not effective. Thus, this case was also important in terms of MF therapy.

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References

1. Weinstein IM: Idiopathic myelofibrosis: Historical review, diagnosis and management. Blood Rev 5:98, 1991.
2. Hasselbalch HC: Idiopathic myelofibrosis—An update with particular reference to clinical aspects and prognosis. Int J Clin Lab Res 23:124, 1993.
3. Betz SA, Foucar K, Head DR, Chen IM, William CL: False-positive flow cytometric platelet glycoprotein IIb/IIIa expression in myeloid leukemias secondary to platelet adherence to blasts. Blood 79:2399, 1992.
4. Reilly JT: Pathogenesis of idiopathic myelofibrosis: Role of growth factors. J Clin Pathol 45:461, 1992.
5. McCarthy DM: Fibrosis of the bone marrow. Content and causes. Br J Haematol 59:1, 1985.

TABLE 1. Changes in Surface Markers of White Cells in Peripheral Blood and Synovia*

Date	10/21	2/27	3/8	4/6	5/2	11/21	12/6	12/13	3/8	5/2	12/9
Mat.	PB	PB	PB	PB	PB	PB	PB	PB	PB	PB	Syn.
Gate	Gr.	Gr.	Gr.	Gr.	Gr.	Mono	Mono	Mono	Mono	Mono	Mono
CD11b	ND	97.5	95.8	98.2	96.6	99.2	94.2	89.6	98.9	98.1	99.6
CD13	ND	89.3	74.0	96.9	90.4	79.9	75.8	81.0	96.4	95.3	81.0
CD14	ND	17.5	>1.0	52.3	3.2	93.0	82.0	ND	13.8	71.5	69.8
CD33	ND	11.2	13.6	97.7	94.9	90.7	72.5	82.2	48.0	99.2	35.8
CD41a	28.1	21.6	10.0	11.7	14.6	77.0	34.0	61.9	43.0	49.0	>1.0

*Mat., material; PB, peripheral blood; Syn., synovia; Gr., granulocyte; Mono, monocyte; ND, not done. Data are shown as positive percentage of gated cells.

Serum Beta-2 Microglobulin as a Marker of B-Cell Activation in Chronic Lymphoid Malignancies

To the Editor: In an attempt to correlate the serum beta-2 microglobulin (β2m) level and the stage of maturation of tumor cells in lymphoid malignancies, we evaluated the β2m levels in 111 patients with chronic lymphoid disorders using a microparticle enzyme immunoassay (Abbott, Abbott Park, IL). Disorders included: prolymphocytic leukemia (PLL) (4 cases), CLL with prolymphocytic features (CLL-PL) 11 cases, typical CLL in various clinical stages (56 cases; 38 in Rai stage 0.1, and 18 in Rai stages 2–4), early myeloma or gammopathy of unknown significance (MGUS) (19 cases), advanced multiple myeloma (21 cases), and 20 normal controls. The level of β2m was significantly higher in patients with PLL (mean 4,421 μg/l, range 3,524–5,580 μg/l) and CLL-PL (mean 3,700 μg/l, range 2,089–6,142 μg/l) compared to controls (mean 1,305, range 803–1,715 μg/l) ($P < 0.01$), early CLL (mean 1,824 μg/l, range 1,040–3,600 μg/l) ($P < 0.01$), advanced stage CLL (mean 2,707 μg/l, range 1,477–4,150 μg/l) ($P < 0.01$), and MGUS and early myeloma (mean 1,714 μg/l, range 1,054–2,805 μg/l) ($P < 0.01$). Highest levels of β2m were observed in the group of advanced myeloma (mean 4,980 μg/l, range 2,600–18,320 μg/l) (Fig. 1).

Beta-2 microglobulin is an 11-kDa protein recognized as the light-chain component of the major histocompatibility complex (MHC) class 1 antigen [1]. It is produced by nucleated cell membranes and is detectable in the serum and other body fluids. The association between the β2m/HLA molecule and membrane structures responsible for lymphocyte activation has been well-defined [2]. The serum β2m level is elevated in a variety of conditions characterized by lymphocyte activation and dysfunction, and

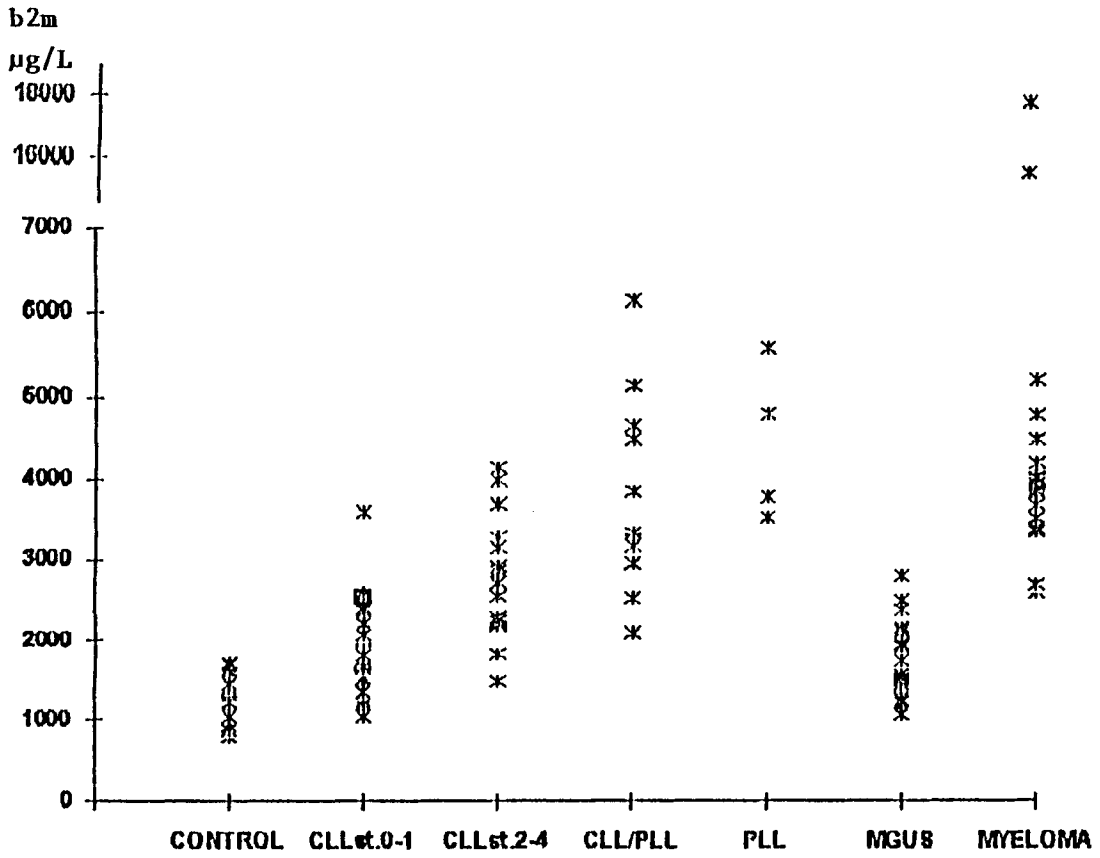

Fig. 1. Values of β2-microglobulin in different groups of patients.